

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 03 May 1999 (03.05.99)	
<b>International application No.</b> PCT/US98/16890	<b>Applicant's or agent's file reference</b> UPAP-0262
<b>International filing date</b> (day/month/year) 14 August 1998 (14.08.98)	<b>Priority date</b> (day/month/year) 14 August 1997 (14.08.97)
<b>Applicant</b> MAHALINGAM, Sundarasamy et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

10 March 1999 (10.03.99)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
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# PATENT COOPERATION TREATY

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JAN 31 2000

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Woodcock Washburn Kurtz  
Mackiewicz & Norris LLP

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: MARK DELUCA  
WOODCOCK WASHBURN KURTZ MACKIEWICZ &  
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## NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing  
(day/month/year)

27 JAN 2000

Applicant's or agent's file reference  
UPAP-0262

### IMPORTANT NOTIFICATION

International application No.  
PCT/US98/16890

International filing date (day/month/year)  
14 AUGUST 1998

Priority Date (day/month/year)  
14 AUGUST 1997

Applicant  
THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

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Authorized officer  
JILL D. MARTIN

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## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference UPAP-0262	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US98/16890	International filing date (day/month/year) 14 AUGUST 1998	Priority date (day/month/year) 14 AUGUST 1997
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant THE TRUSTEES OF THE UNIVERSITY OF PENNSYLVANIA		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand  10 MARCH 1999	Date of completion of this report  03 DECEMBER 1999
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer  JILL D. MARTIN Telephone No. (703) 308-0198

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/16890

## I. Basis of the report

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments)*:

- ☒ the international application as originally filed.
- ☒ the description, pages 1-42 , as originally filed.  
pages NONE , filed with the demand.  
pages NONE , filed with the letter of \_\_\_\_\_.  
pages \_\_\_\_\_ , filed with the letter of \_\_\_\_\_.
- ☒ the claims, Nos. 1-27 , as originally filed.  
Nos. NONE , as amended under Article 19.  
Nos. NONE , filed with the demand.  
Nos. NONE , filed with the letter of \_\_\_\_\_.  
Nos. \_\_\_\_\_ , filed with the letter of \_\_\_\_\_.
- ☒ the drawings, sheets/fig 1-12 , as originally filed.  
sheets/fig NONE , filed with the demand.  
sheets/fig NONE , filed with the letter of \_\_\_\_\_.  
sheets/fig \_\_\_\_\_ , filed with the letter of \_\_\_\_\_.

2. The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE .
- ☒ the claims, Nos. NONE .
- ☒ the drawings, sheets/fig NONE .

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/16890

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims <u>1-27</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>12-27</u>	YES
	Claims <u>1-11</u>	NO
Industrial Applicability (IA)	Claims <u>1-27</u>	YES
	Claims <u>NONE</u>	NO

**2. CITATIONS AND EXPLANATIONS**

Claims 1-11 lack an inventive step under PCT Article 33(3) as being obvious over The Trustees of the University of Pennsylvania (WO 96/08970).

The claims are directed to conjugated compositions comprising amino acid sequences 17-36 or 59-84 of HIV-1 Vpr conjugated to a therapeutic compound.

The Trustees of the University of Pennsylvania disclose the concept of using vpr for delivery of agents of interest into the cell nucleus. Specifically, nucleic acid-vpr conjugates are disclosed. See paragraph bridging pages 36-37. Other agents of interest include drugs, radioisotopes, and protein based toxins. The Trustees of the University of PA further disclose that one can readily design dimers crosslinked with crosslinking agents or disulfide bonds, etc. Furthermore, fragments of vpr which bind to rip-1 comprise vpr residues 27-39, 35-48, 41-55, 49-60, and/or 66-68.

Accordingly, it would have been obvious for one of ordinary skill in the art, at the time of the invention, to construct conjugated compositions comprising various regions encompassing the known residues which bind to rip-1 and conjugate them with a therapeutic agent for delivery to the cell nucleus with a reasonable expectation of success.

Claims 12-27 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest methods of inhibiting cell proliferation utilizing vpr or methods of identifying compounds that inhibit vpr binding to p6 domain of p55 or to p6 protein.

Claims 1-27 meet the criteria set out in PCT Article 33(4), because the claimed invention is useful in delineating the relationship between different functions of vpr.

----- NEW CITATIONS -----

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/16890

**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

**CLASSIFICATION:**

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(6): G01N 33/53; C12P 21/06; C12N 15/00, 15/63; A01N 43/04; A61K 31/70 and US Cl.: 436/501; 435/7.1, 7.8, 69.1, 455